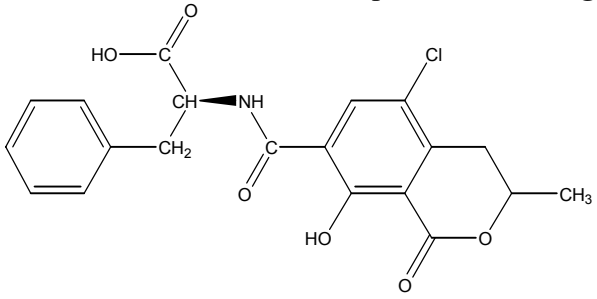
OCHRATOXIN A
CAS No. 303-47-9
First Listed in the *Sixth Annual Report on Carcinogens*



CARCINOGENICITY

Ochratoxin A is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals. When administered by gavage, ochratoxin A substantially increased the incidence of uncommon tubular cell adenomas and of tubular cell carcinomas of the kidney in male and female rats. Ochratoxin A also increased the incidence and multiplicity of fibroadenomas of the mammary gland in female rats (NTP 358, 1989). When ochratoxin A was administered in the diet, renal adenomas and carcinomas were observed in male mice, and some hepatocellular carcinomas were observed in female mice in one study. In another study, administration of ochratoxin A in the diet induced hepatomas and renal cell tumors in male mice. Other studies by dietary administration and studies by subcutaneous injection to mice and rats were considered inadequate in terms of the numbers of animals used and survival rates by an IARC Working Group. Based on these observations, the IARC Working Group considered the evidence for the carcinogenicity of ochratoxin A to be limited. The IARC Working group had not yet evaluated the NTP data (IARC V.31, 1983; IARC S.7, 1987; NTP 358, 1989). In view of a NCI/OTA correlative interpretation, the evidence may be regarded as sufficient (Griesemer & Cueto, 1980; OTA, 1981).

There are no adequate data available to evaluate the carcinogenicity of ochratoxin A in humans. Incidence of and mortality from urothelial urinary tract tumors have been correlated with the geographical distribution of Balkan endemic nephropathy in Bulgaria and Yugoslavia. A relatively high frequency of contamination of cereals and bread with ochratoxin A has been reported in an area of Yugoslavia where Balkan endemic nephropathy is present. No report of a direct association between ochratoxin A and human cancer is available (IARC V.10, 1976; IARC V.31, 1983; IARC S.7 1987).

PROPERTIES

Ochratoxin A is a toxic metabolite produced primarily by *Aspergillus* but also by *Penicillium* and other molds. It is a white crystalline powder. Recrystallized from xylene, it forms crystals that emit green (acid solution) and blue (alkaline solution) fluorescence in ultraviolet light; the melting point of these crystals is 169°C. The free acid of ochratoxin A is soluble in polar organic solvents (IARC V.31, 1983). The sodium salt is soluble in water. Ochratoxin A is unstable to light and air, degrading and fading even after brief exposure to light especially under humid conditions. Ethanol solutions are stable for longer than 1 year if kept in the dark and cold. Ochratoxin A is fairly stable to heat; in cereal products, up to 35% of the toxin survives autoclaving for up to 3 hours. When heated to decomposition, the toxin emits

toxic fumes of chlorine and NO_x. It is incompatible with strong oxidizing agents, strong acids, and strong bases.

USE

The toxin has no known commercial use but is an experimental teratogen and carcinogen (IARC V.31, 1983; Sax and Lewis, 1987).

PRODUCTION

Ochratoxin A is not produced commercially; however, it was previously offered for sale by one foreign firm (IARC V.10, 1976).

EXPOSURE

Ochratoxin A is a naturally occurring mycotoxin. It exists completely in particulate phase in ambient atmosphere. It is immobile in soil. Its widespread occurrence in food and animal feed results in probable human exposure. Mycotoxins may well be among the world's most significant food contaminants (Fischbach and Rodricks, 1973). Ochratoxin-producing fungi are included in the Penicillium and Aspergillus genera (IARC V.10, 1976). In the colder climates, ochratoxin A is formed by Penicillium strains and in tropical and subtropical areas, by Aspergillus. Ochratoxin A is a natural contaminant on corn, peanuts, storage grains, cottonseed, and decaying vegetation (Merck, 1989). It has been detected in moldy cereals including wheat, maize, rye, barley, and oats; peanuts; coffee beans; bread; flour; rice; peas; and beans (IARC V.31, 1983). Detected contamination levels in cereals range from 0.03 ppm to 27.5 ppm (Scott et al., 1972; Krogh et al., 1973). Although the carryover from barley into beer is possible, one survey of all 130 U.S. breweries did not detect ochratoxin A (up to 10 µg/kg) in beer or malted barley (Fischbach and Rodricks, 1973; IARC V.31, 1983). The malting process completely degrades the toxin in moderately contaminated barley, but 2%-7% of the toxin was carried over to the final product from a heavily contaminated lot (Krogh et al., 1974; IARC, 1983). Up to 28% of added toxin was detected in a final beer product (Chu et al., 1975).

Residues of ochratoxin A have been detected in samples of meat from animals slaughtered immediately after consuming contaminated feed (Krogh, 1977; IARC V.31, 1983). It has been detected at levels of 10-920 µg/kg in sausage, ham, and bacon samples (IARC V.31, 1983).

No direct evidence of worker exposure has been reported. Potential worker exposure exists for all personnel handling and storing grains, nuts, corn, cereals, and animal feeds.

REGULATIONS

OSHA regulates ochratoxin A under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-114.